09-J0000-94

Original Effective Date: 04/15/09

Reviewed: 07/09/25

Revised: 06/01/26

Next Review: 07/08/26

Subject: Human EGFR Inhibitors (Cetuximab [Erbitux®], Panitumumab [Vectibix®])

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Position Statement	Dosage/ Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Cetuximab (Erbitux®) and panitumumab (Vectibix®) are human monoclonal antibodies that target the epidermal growth factor receptor (**EGFR**, also known as HER-1). EGFR is expressed in many normal epithelial tissues, including the skin and hair follicle. Over expression of EGFR has been detected in many human cancers including those of the head and neck, colon and rectum. Excessive activation of EGFR is associated with advanced stages of cancer and a poor prognosis. In contrast to small molecule tyrosine kinase inhibitors (e.g., imatinib [Gleevec®]) that inhibit EGFR by interfering with ATP binding, cetuximab and panitumumab block the EGFR receptor on both normal and cancerous cells. This binding blocks phosphorylation and activation of receptor-associated kinases, resulting in inhibition of cell growth, induction of apoptosis, and decreased survival of tumor cells that express the EGFR. Panitumumab differs from cetuximab in that it has a higher affinity for the receptor and it produces less hypersensitivity reactions.

The FDA approved cetuximab with irinotecan for KRAS mutation negative (wild type), EGFR-expressing metastatic colorectal cancer (mCRC) refractory to irinotecan-based chemotherapy and as a single agent for patients who are intolerant of irinotecan-based chemotherapy. The indication was expanded as monotherapy for mCRC after failure of both irinotecan- and oxaliplatin-based regimens, and approved as first-line therapy in combination with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin). It is also FDA approved for squamous cell head and neck cancer as a single agent for recurrent or metastatic disease following platinum-based therapy, with radiation therapy as initial therapy for locally or regionally advanced disease, or in combination with platinum-based chemotherapy and fluorouracil as first-line therapy of recurrent or metastatic disease.

The FDA approved panitumumab for the treatment of patients with wild-type KRAS/NRAS metastatic colorectal cancer (mCRC) as monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy. The indication was expanded to include use in combination with FOLFOX for first-line treatment wild-type KRAS/NRAS mCRC. It is also FDA-approved in combination with sotorasib for the treatment of adult patients with KRAS G12C-mutated

metastatic colorectal cancer who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

Current National Comprehensive Cancer Network (NCCN) guidelines support the use of cetuximab in colorectal cancer, squamous cell carcinoma of the head and neck, non-melanoma carcinoma of the skin, non-small cell lung cancer, and penile cancer. NCCN guidelines support the use of panitumumab in colorectal cancer.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline Drug Waste Reduction, 09-J5000-54.

Initiation of cetuximab (Erbitux®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Cetuximab is used to treat any of the indications listed in table 1.
2. All of the indication-specific criteria are met.
3. The member has not previously experienced disease progression during treatment with cetuximab [Erbitux®]
4. Cetuximab is **NOT** used in combination with **ANY** of the following:
    a. Bevacizumab (Avastin®)
    b. Erlotinib (Tarceva®)
    c. Gefitinib (Iressa®)
    d. Panitumumab (Vectibix®)
5. The dose of cetuximab does not exceed either of the following:
    - 400 mg/m^2 initially, then 250 mg/m^2 every 7 days
    - 500 mg/m^2 every 14 days

Table 1:

Indications and Specific Criteria	
Indication	**Criteria**
Colorectal cancer (includes appendiceal adenocarcinoma)	When **ALL** of the following are met: a. Member's disease is classified as **ONE** of the following: a. Unresectable b. Advanced c. Medically inoperable d. Metastatic b. **ONE** of the following: a. When KRAS/NRAS/BRAF gene is normal (i.e., without mutation or wild type) and used as a single agent or in combination with **ONE** of the following: i. CapeOx (capecitabine and oxaliplatin)

	ii. Irinotecan iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin) iv. FOLFIRI (fluorouracil, leucovorin, irinotecan) b. When BRAF V600E mutation positive and used in combination with **ONE** of the following: i. encorafenib (Braftovi) ii. encorafenib (Braftovi) and FOLFOX (fluorouracil, leucovorin, oxaliplatin) c. When KRAS G12C mutation positive and used in combination with sotorasib (Lumakras) or adagrasib (Krazati) d. When classified as microsatellite instability-high [MSI-H], mismatch repair deficient [dMMR], or POLE/POLD1 mutation positive with ultrahypermutated phenotype [e.g., TMB>50 mut/Mb] and ineligible for or progressed on checkpoint inhibitor immunotherapy when used as a single agent or in combination with **ONE** of the following: i. CapeOx (capecitabine and oxaliplatin) ii. Irinotecan iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin) iv. FOLFIRI (fluorouracil, leucovorin, irinotecan) v. sotorasib (Lumakras) or adagrasib (Krazati) when KRAS G12C mutation positive vi. encorafenib (Braftovi) when BRAF V600E mutation positive vii. encorafenib (Braftovi) and FOLFOX when BRAF V600E mutation positive
Head and Neck Cancer	Cetuximab will be used for **ONE** of the following: 1. For squamous cell head and neck cancer (SCCHN) when used as a single agent or in combination with **ONE** of the following: a. Radiation therapy b. Platinum therapy (i.e., cisplatin or carboplatin) c. Platinum therapy and ONE of the following: 1. Docetaxel 2. Fluorouracil 3. Paclitaxel d. Nivolumab e. Pembrolizumab f. Paclitaxel 2. For head and neck cancer when used as a single agent or in combination with radiation therapy

Non-small cell lung cancer (NSCLC)	When used in combination with afatinib for recurrent, advanced, or metastatic disease **AND** member's disease has progressed on EGFR tyrosine kinase inhibitor therapy (e.g., erlotinib, gefitinib, osimertinib, dacomitinib, lazertinib)
Penile cancer	When **ALL** of the following apply: 1. Disease is metastatic or recurrent 2. Member had an inadequate response to initial chemotherapy 3. Used as single-agent therapy
Squamous cell skin cancer	Member has squamous cell skin cancer and member's disease is classified as **ONE** of the following: 1. Unresectable or incompletely resected 2. Medically inoperable 3. Locally advanced 4. Resected high-risk regional disease 5. Recurrent 6. Metastatic
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When **ALL** of the following are met: 1. **ONE** of the following is met: a. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) b. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
Approval duration: 6 months	

Continuation of cetuximab (Erbitux®) **meets the definition of medical necessity** for the treatment any indication in Table 1 when **ALL** of the following criteria are met:

1. An authorization/reauthorization for cetuximab has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member previously met all indication-specific initiation criteria.
2. The member has not experienced disease progression during treatment with cetuximab.
3. Cetuximab is **NOT** used in combination with **ANY** of the following:
    A. Bevacizumab (Avastin®)
    B. Erlotinib (Tarceva®)
    C. Gefitinib (Iressa®)
    D. Panitumumab (Vectibix®)
4. The dose does not exceed 250 mg/m^2 every 7 days or 500 mg/m^2 every 14 days.

Approval duration: 1 year

Initiation of panitumumab (Vectibix®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Colon or rectal cancer (includes appendiceal carcinoma)
    A. Member's disease is classified as **ONE** of the following:
        a. Unresectable
        b. Advanced
        c. Medically inoperable
        d. Metastatic
    B. **ONE** of the following:
        a. When KRAS/NRAS/BRAF gene is normal (i.e., without mutation or wild type) and used as a single agent or in combination with **ONE** of the following:
            i. CapeOx (capecitabine and oxaliplatin)
            ii. Irinotecan
            iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
            iv. FOLFIRI (fluorouracil, leucovorin, irinotecan)
        b. When BRAF V600E mutation positive and **ONE** of the following:
            i. encorafenib (Braftovi)
            ii. encorafenib (Braftovi) and FOLFOX (fluorouracil, leucovorin, oxaliplatin)
        c. When KRAS G12C mutation positive and used in combination with sotorasib (Lumakras) or adagrasib (Krazati)
        d. When classified as microsatellite instability-high [MSI-H], mismatch repair deficient [dMMR], or POLE/POLD1 mutation positive with ultrahypermutated phenotype [e.g., TMB>50 mut/Mb] and ineligible for or progressed on checkpoint inhibitor immunotherapy when used as a single agent in combination with **ONE** of the following:
            i. CapeOx (capecitabine and oxaliplatin)
            ii. Irinotecan
            iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
            iv. FOLFIRI (fluorouracil, leucovorin, irinotecan)
            v. sotorasib (Lumakras) or adagrasib (Krazati) when KRAS G12C mutation positive
            vi. encorafenib (Braftovi) when BRAF V600E mutation positive
            vii. encorafenib (Braftovi) and FOLFOX when BRAF V600E mutation positive
    C. The member has not previously experienced disease progression during treatment with panitumumab [Vectibix®]
    D. Panitumumab is **NOT** used in combination with **ANY** of the following:
        a. Bevacizumab (Avastin®)
        b. Cetuximab (Erbitux®)
        c. Erlotinib (Tarceva®)

d. Gefitinib (Iressa®)

E. The dosage does not exceed 6 mg/kg every 14 days.

2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)

A. **ONE** of the following is met:

a. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

b. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

B. The dose does not exceed the maximum FDA-approved dose

Approval duration: 6 months

Continuation of panitumumab (Vectibix®) **meets the definition of medical necessity** for the treatment of colon or rectal cancer, or other FDA-approved or NCCN supported diagnosis when **ALL** of the following criteria are met:

1. An authorization/reauthorization for panitumumab has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member previously met all indication-specific initiation criteria.
2. The member has not experienced disease progression during treatment with panitumumab
3. Panitumumab is **NOT** used in combination with **ANY** of the following:
    a. Bevacizumab (Avastin®)
    b. Cetuximab (Erbitux®)
    c. Erlotinib (Tarceva®)
    d. Gefitinib (Iressa®)
4. The dosage does not exceed 6 mg/kg every 14 days.

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approval:

- Cetuximab: cetuximab is FDA-approved for treatment of head and neck cancer and colorectal cancer in the following settings
    - Squamous cell Carcinoma of the Head and Neck
        - Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
            - In combination with radiation;

        - The recommended dose is 400 mg/m^2 initially as an intravenous (IV) infusion over 120 minutes one week prior to initiating a course of radiation
        - The subsequent dose is 250 mg/m^2 weekly IV over 60 minutes for the duration of radiation (6-7 weeks) and administered 1 hour prior to radiation.
    - Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with 5-FU.
    - Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy as monotherapy.
        - As a single agent or in combination with platinum-based therapy with 5-FU and FOLFIRI.
            - The recommended dose is 400 mg/m^2 initially as an intravenous (IV) infusion over 120 minutes followed by 250 mg/m^2 weekly IV over 60 minutes.
            - Biweekly dosing is administered as 500 mg/m^2 as a 120-minute IV infusion every 2 weeks
            - Cetuximab administration should be completed 1 hour prior to chemotherapy
            - Continue treatment until disease progression or unacceptable toxicity

- Colorectal Cancer:
    - KRAS mutation-negative (wild-type), EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved tests
        - in combination with FOLFIRI for first-line treatment,
        - in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
        - as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan
            - As a single agent or in combination with irinotecan or FOLFIRI.
                - The recommended dose is 400 mg/m^2 initially as an intravenous (IV) infusion over 120 minutes followed by 250 mg/m^2 weekly IV over 60 minutes
                - Biweekly dosing is administered as 500 mg/m^2 as a 120-minute IV infusion every 2 weeks
                - Cetuximab administration should be completed 1 hour prior to chemotherapy
                - Continue treatment until disease progression or unacceptable toxicity
        - Cetuximab is not indicated for treatment of persons with RAS mutation-positive mCRC
    - BRAF V600E mutation-positive metastatic colorectal cancer (CRC)
        - In combination with encorafenib, 400 mg/m^2 initially as an intravenous (IV) infusion over 120 minutes followed by 250 mg/m^2 weekly IV over 60 minutes.

- Prior to cetuximab therapy, members should be pre-medicated with a histamine-receptor antagonist.
- See prescribing information for adverse reactions that may require reduction of infusion rate or dose, withholding treatment or permanent discontinuation.

- Panitumumab is indicated for the treatment of patients with colorectal cancer with the following:
  - Wild-type RAS (KRAS and NRAS) metastatic colorectal cancer (mCRC) as determined by an FDA-approved test for this use:
    - As first-line therapy in combination with FOLFOX
    - As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy. Panitumumab is not indicated for treatment of persons with *RAS* mutation-positive mCRC or for persons who *RAS* mCRC status is unknown.
  - KRAS G12C-mutated mCRC
    - In combination with sotorasib following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.
  - The recommended dose is 6 mg/kg every 14 days. Panitumumab should be administered as an IV infusion over 60 minutes (doses of 1000 mg or less) or 90 minutes (doses greater than 1000 mg).
  - Infusion reactions may occur; appropriate medical resources for the treatment of infusion reactions should be available.
  - Withhold or discontinue for severe or intolerant dermatologic reactions. Reduce dose for recurrent, grade 3 toxicity.

Drug Availability

- Cetuximab is supplied as 100 mg/50 mL and 200 mg/100 mL single-use vials. Store vials under refrigeration at 2° C to 8° C (36° F to 46° F).
- Panitumumab is supplied as 100 mg/5 mL and 400 mg/20 mL single-use vials. Store vials in the original carton under refrigeration at 2º to 8ºC (36º to 46ºF) until time of use. Protect from direct sunlight.

PRECAUTIONS:

Boxed Warning

- **Cetuximab**
  - **Serious infusion reactions may occur.** Immediately stop and permanently discontinue cetuximab if a serious reaction occurs.
  - **Cardiopulmonary arrest and/or sudden death** have been reported by persons administered cetuximab. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after cetuximab administration
- **Panitumumab**
  - **Dermatologic toxicities may occur**. Withhold or discontinue panitumumab if severe or life-threatening complications occur. Limit sun exposure

Warnings and Precautions

- **Cetuximab**

- **Infusion reactions: see boxed warning**. The risk of anaphylactic reactions may be increased in patients with a history of tick bites, red meat allergy, or in the presence of IgE antibodies directed against alpha-gal. Consider testing patient for alpha-gal IgE antibodies using FDA-cleared methods prior to initiating treatment.
- **Cardiopulmonary arrest**: see boxed warning.
- **Pulmonary Toxicity:** Interrupt therapy for acute onset or worsening of pulmonary symptoms.
- **Dermatologic Toxicity:** Mucocutaneous adverse reactions. Limit sun exposure. Monitor for inflammatory or infectious sequelae.
- **Increased risk of adverse reactions associated with combined use of radiation and cisplatin**: see prescribing information.
- **Hypomagnesemia:** Periodically monitor during and for at least 8 weeks following the completion of cetuximab. Replete electrolytes as necessary.
- **Increased tumor progression**, increased mortality or lack of benefit when used in patients with RAS-mutant metastatic colorectal cancer
- **Embryo-fetal toxicity**: Can cause fetal harm. Advise females to use contraceptives and of the potential risk to the fetus.

- **Panitumumab**
  - **Dermatologic and soft tissue toxicities may occur**. Withhold or discontinue panitumumab if severe or life-threatening complications occur. Limit sun exposure
  - **Increased tumor progression, increased mortality or lack of benefit** when panitumumab is used in patients with RAS-mutant metastatic colorectal cancer
  - **Pulmonary Fibrosis/Interstitial Lung Disease (ILD):** Permanently discontinue panitumumab in persons developing ILD.
  - **Electrolyte Depletion/Monitoring:** Monitor electrolytes during and for 8 weeks after completion of panitumumab therapy and institute appropriate treatment.
  - **Infusion reactions**: Immediately stop and permanently discontinue if serious infusion reaction occurs.
  - **Ocular Toxicities**: Monitor for evidence of keratitis, ulcerative keratitis, or corneal perforation. Interrupt or discontinue panitumumab for acute or worsening keratitis, ulcerative keratitis, or corneal perforation.
  - **Embryo-fetal toxicity**: Can cause fetal harm. Advise females to use contraceptives and of the potential risk to the fetus.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J9055	Injection, cetuximab,10 mg
J9303	Injection, panitumumab,10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity for J9055 (cetuximab):

C00.0 – C08.9	Malignant neoplasm of lip, base of tongue, of other and unspecified parts of tongue, gum, floor of mouth, palate, of other and unspecified parts of mouth, parotid and salivary gland.

C09.0 – C10.9	Malignant neoplasm of tonsil and oropharynx
C11.0 – C11.9	Malignant neoplasm of nasopharynx
C12.0 – C14.8	Malignant neoplasm of piriform sinus, hypopharynx and other and ill-defined sites in the lip, oral cavity and pharynx.
C17.0 – 17.2	Malignant neoplasm of duodenum, jejunum, ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0 – C21.8	Malignant neoplasm of colon, rectosigmoid junction, rectum and anus and anal canal
C30.0	Malignant neoplasm of nasal cavity
C31.0 – C31.9	Malignant neoplasm of accessory sinuses
C32.0 – C34.92	Malignant neoplasm of larynx, trachea, bronchus and lung
C44.00	Malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C44.121 – C44.1292	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.221 – C44.229	Squamous cell carcinoma of skin of unspecified ear and external auricular
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.42	Squamous cell carcinoma of skin of scalp and neck
C44.520	Squamous cell carcinoma of anal skin
C44.521	Squamous cell carcinoma of skin of breast
C44.529	Squamous cell carcinoma of skin of other part of trunk
C44.621 – C44.629	Squamous cell carcinoma of skin of unspecified upper limb, including shoulder
C44.721 – C44.729	Squamous cell carcinoma of skin of unspecified lower limb, including hip
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.92	Squamous cell carcinoma of skin, unspecified
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C60.0 – C60.9	Malignant neoplasm of penis
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C72.1	Malignant neoplasm of cauda equina
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.00 – C78.02	Secondary malignant neoplasm of unspecified lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.04	Neoplasm of uncertain behavior of the minor salivary glands
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified

ICD-10 Diagnoses Codes That Support Medical Necessity for J9303 (panitumumab):

C17.0 – 17.2	Malignant neoplasm of duodenum, jejunum, ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine

C17.9	Malignant neoplasm of small intestine, unspecified
C18.0 – C21.8	Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal
C78.00 – C78.89	Secondary malignant neoplasm of respiratory and digestive organs

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: The following National Coverage Determination (NCD) was found at the time of the last guideline revised date: Anti-cancer chemotherapy for colorectal cancer, (110.17). No Local Coverage Determination (LCD) was found on the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Apoptosis: A state in which a cell has ceased replication and is in the process of programmed cell death.

EGFR: The epidermal growth factor receptor (EGFR; ErbB-1; HER1 in humans) is the cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands. The epidermal growth factor receptor is a member of the ErbB family of receptors, a subfamily of four closely related receptor tyrosine kinases: EGFR (ErbB-1), HER2/c-neu (ErbB-2), Her 3 (ErB-3) and Her 4 (ErB-4). Mutations affecting EGFR expression or activity could result in cancer.

FOLFOX: combination chemotherapy consisting of the following agents; leucovorin, fluorouracil, oxaliplatin.

FOLFIRI: combination chemotherapy consisting of the following agents; leucovorin, fluorouracil, irinotecan.

RELATED GUIDELINES:

Analysis of Human DNA in Stool Samples as a Technique for Colorectal Cancer Screening, 05-82000-27

Bevacizumab (Avastin®) Injection, 09-J0000-66

Docetaxel (Taxotere®s) IV, 09-J0000-95

Gemcitabine (Gemzar®), 09-J0000-96

KRAS Mutation Analysis, 05-86000-28

Oxaliplatin (Eloxatin®) IV, 09-J1000-00

Paclitaxel and Paclitaxel (protein-bound) IV, 09-J1000-05

Topotecan HCl (Hycamtin®) IV, 09-J1000-02

Vinorelbine Tartrate (Navelbine®) IV, 09-J1000-03

OTHER:

TABLE 1

ECOG PERFORMANCE STATUS	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

REFERENCES:

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2. Clinical Pharmacology. [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Accessed 06/27/25
3. Erbitux (cetuximab) [package insert]. Bristol-Myers Squibb Co. Princeton (NJ): September 2021.
4. Micromedex ® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 06/27/25.
5. Mrabti H, La Fouchardiere C, Desseigne F, et al. Irinotecan associated with cetuximab given every 2 weeks versus cetuximab weekly in metastatic colorectal cancer. J Can Res Ther. 2009;5:272-6.
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7. Pfeiffer P, Bjerregarrd JK, Qvortrup C, et al, “Simplification of Cetuximab (Cet) Administration: Double Dose Every Second Week as a 60 Minute Infusion,” J Clin Oncol, 2007, 25(18S):4133 [abstract 4133 from 2007 ASCO Annual Meeting Proceedings, Part I].
8. Vectibix (panitumumab) [package insert]. Amgen Inc. Thousand Oaks (CA): January 2025.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/09/25.

GUIDELINE UPDATE INFORMATION:

04/15/09	New Medical Coverage Guideline.
05/15/09	Revision to guideline; consisting of adding panitumumab coverage criteria, updating ICD-9 codes for cetuximab, changing name and updating references.
10/15/09	Revision to guideline; consisting of clarifying dosage.
04/15/10	Revision to guideline; consisting of updating codes.
08/01/10	Revision to guideline; consisting of updating codes.
09/15/10	Review and revision to guideline; consisting of updating coding and references.
09/15/11	Review and revision to guideline; consisting of updating coding and references.
10/01/11	Revision to guideline; consisting of updating codes.

09/15/12	Review and revision to guideline; consisting of updating position statement, precautions, coding and references.
12/15/12	Revision to guideline; consisting of updating coding.
09/15/13	Review and revision to guideline; consisting of revising and reformatting position statement; revising description, dosage/administration and precautions sections; updating references, program exceptions, and coding.
02/15/14	Revision to guideline; consisting of removing chordoma indication.
08/15/14	Review and revision to guideline; consisting of reformatting position statement, updating dosage/administration and references.
08/15/15	Review and revision to guideline; consisting of description, position statement, and references.
09/15/15	Revision to guideline consisting of revised dosage in position statement and references.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.
08/15/16	Review and revision to guideline; consisting of updating description, position statement, coding and references.
10/15/16	Revision to guideline consisting of updating position statement and references.
08/15/17	Revision to guideline consisting of updating position statement, coding, and references.
03/15/18	Revision to guideline consisting of updating position statement and references.
07/15/18	Review and revision to guideline; consisting of updating the position statement, warnings, coding and references.
05/15/19	Revision to guideline; consisting of updating the position statement, coding and references.
08/15/19	Review and revision to guideline; consisting of updating references.
02/15/20	Revision to guideline; consisting of updating the position statement and references.
08/15/20	Review and revision to guideline; consisting of updating the position statement and references.
08/15/21	Review and revision to guideline; consisting of updating the position statement and references.
08/15/22	Review and revision to guideline; consisting of updating the position statement and references.
10/15/23	Review and revision to guideline; consisting of updating the position statement to include updates to head and neck cancer, colorectal cancer, NSCLC, and Squamous cell skin cancer.
10/15/24	Review and revision to guideline; consisting of updating the position statement with NCCN updates for appendiceal cancer, colorectal cancer, head and neck cancer, penile cancer and Squamous cell skin cancer.
08/15/25	Review and revision to guideline; consisting of updating the position statement with NCCN updates for colorectal cancer.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.